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## **LEGIONELLA INFECTIONS**

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The 58<sup>th</sup> annual convention of the American Legion's Pennsylvania Department took place at the Bellevue Stanford Hotel in Philadelphia, July 21-24 1976. Starting July 22 convention attendees and other individuals who had entered the hotel became sick. The main clinical presentation was a pneumonia. All in all there were 182 cases identified plus an additional 39 cases among people who had been in the same block where the hotel was located. Among the 221 cases, there were 34 deaths. Six months later a small bacterium named *Legionella pneumophila* was isolated from guinea pigs inoculated with the lung tissues of the cases.

Similar agents had been isolated before but never before so thoroughly characterized: in 1943 *L. micdadei* from the blood of a febrile soldier in Fort Bragg, NC; in 1959 *L. bozemannii* from the lung tissue of a scuba diver; It was also identified as the causative for Pontiac fever, an outbreak of acute febrile illness that occurred in 1968 in the Michigan Health Department building in Pontiac.

Legionnaires' disease is a multisystem illness, with pneumonia, caused by *Legionella spp.* In contrast, Pontiac fever is a self-limited influenza-like illness, without pneumonia, that is associated with *Legionella spp.*

*Legionella* are small (0.3-0.9  $\mu$ ) bacteria which looks like very small Gram negative bacteria. They do NOT grow on standard bacteriologic media. Buffered charcoal yeast extract agar is the base medium used. It is supplemented by antibiotics to prevent overgrowth of *Legionella* and a dye to give *Legionella* a distinctive color. The microorganism grows slowly, 3-5 days to have small colonies.

At least 18 different species have been implicated in human disease, but the majority of *Legionella* infections in the United States are caused by the *Legionella pneumophila* serogroup 1.

In nature, *Legionella* infect free living amoebae (as *Acanthamoeba*, *Naegleria* and *Harmanella*). They multiply within the amoebae. They do not seem to colonize the respiratory tract.

### **Epidemiology**

*Legionella* is not transmitted from person to person. It is always acquired from the environment. Almost all outbreaks of Legionnaire's disease for which an environmental source has been identified were due to inhalation of contaminated aerosolized water.

Inhalation of aerosols of water contaminated with *Legionella spp.* is believed to be the primary mechanism of entry of these organisms into a patient's respiratory tract. Patients are thought to be infected through exposure to contaminated aerosols generated by cooling towers, showers, faucets, respiratory therapy equipment, and room-air humidifiers. In several studies, aspiration of contaminated potable water has been proposed as the mode of transmission to certain patients.

There is no person-to-person transmission.

*Legionella* preferred habitat is water, preferably warm waters with scale, sediment, metallic ions and commensal flora. It is well adapted to the hot water distribution system in dwellings. It can colonize hot water heaters, storage tanks, pipes, shower heads, plumbing materials, faucet aerators and also air-conditioning cooling towers and evaporative condensers. *Legionella* was found in 1-30% of home hot water systems.

Persons with severe immunosuppression or chronic underlying illnesses, such as hematologic malignancy or end-stage renal disease, are at markedly increased risk for legionellosis. Persons in the later stages of acquired immunodeficiency syndrome are also probably at increased risk of legionellosis, but data are limited because of infrequent testing of patients. Persons with diabetes mellitus, chronic lung disease, or non-hematologic malignancy, those who smoke cigarettes, and the elderly are at moderately increased risk.

Legionnaires' Disease Associated With Soil: Infections with one species, *Legionella longbeachae*, have been associated with gardening and use of potting soil in Australia and Japan and recently in the USA. *L. longbeachae* is reported less frequently.

Retrospective and prospective studies show that the *Legionella* were among the most frequent causes of both sporadic or epidemic pneumonias: from 1 to 5% depending on the geographic setting.

The incubation period for legionnaires disease (pneumonia) is 2 to 10 days; for Pontiac fever, it is 1 to 2 days.

### **Clinical Description**

*Legionella* infection causes a wide range of clinical response: asymptomatic serologic conversion, self limited febrile illness with headache, chills and myalgias without pneumonia (Pontiac fever) or progressive and severe pneumonia (Legionnaire's disease). Legionnaire's disease cannot be distinguished clinically or radiologically from other pneumonias.

### **Laboratory Tests**

A diagnosis of legionellosis may be confirmed by:

- Isolation of *Legionella* from respiratory secretion cultures,
- Visualization of *Legionella* in respiratory secretions or tissue by immunofluorescence,
- Detection of *Legionella* serogroup 1 antigens in the urine by radioimmunoassay,
- Four fold rise in antibody titer to *Legionella* rising to above 1:128 in paired sera.

A single elevated antibody titer does not confirm a case of recent legionellosis. 1-16% of adults have IFA titers  $\geq 1:256$

Because the above tests complement each other, performing each test when Legionnaires' disease is suspected increases the probability of confirming the diagnosis. However, because none of the laboratory tests is 100% sensitive, the diagnosis of legionellosis is not ruled out even if one or more of the tests are negative. Of the available tests, the most specific is culture isolation of *Legionella* spp. from any respiratory tract specimen.

### **Treatment**

Macrolides are the antibiotics of choice:

- Erythromycin 1g IV q6hrs or 500mg po qid
- Azithromycin 500mg po qd

- Clarithromycin 500mg po bid

Alternative antibiotics are Rifampin, trimethoprim-sulfamethoxazole, doxycycline, ciprofloxacin.

Intravenous high-dose therapy generally is given initially. Once the patient's condition is improving, oral therapy can be substituted. The addition of rifampin (15 mg/kg per day; maximum, 600 mg/d) is recommended for patients with confirmed disease who are severely ill or immunocompromised or in whom the infection does not respond promptly to intravenous erythromycin. Azithromycin also is effective; intravenous azithromycin may be substituted for intravenous erythromycin. Ciprofloxacin, ofloxacin, and levofloxacin are effective but are not approved for persons younger than 18 years of age. Doxycycline and trimethoprim-sulfamethoxazole are alternative drugs. Duration of therapy is 2 weeks for patients with mild disease and 3 weeks for patients who are immunocompromised or have severe disease.

## **Surveillance**

Legionella illness is a condition reportable within one business day.

## **Case Definition**

### Clinical description

Legionellosis is associated with two clinically and epidemiologically distinct illnesses: Legionnaires disease, which is characterized by fever, myalgia, cough, pneumonia, and Pontiac fever, a milder illness without pneumonia.

### Laboratory criteria for diagnosis

- Isolation of *Legionella* from respiratory secretions, lung tissue, pleural fluid, or other normally sterile fluids, or
- Demonstration of a fourfold or greater rise in the reciprocal immunofluorescence antibody (IFA) titer to greater than or equal to 128 against *Legionella pneumophila* serogroup 1 between paired acute- and convalescent-phase serum specimens, or
- Detection of *L. pneumophila* serogroup 1 in respiratory secretions, lung tissue, or pleural fluid by direct fluorescent antibody testing, or
- Demonstration of *L. pneumophila* serogroup 1 antigens in urine by radioimmunoassay or enzyme-linked immunosorbent assay

### Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment: The previously used category of "probable case," which was based on a single IFA titer, lacks specificity for surveillance and is no longer used.

## **Intervention**

The purpose of investigation is to identify and confirm cases, to identify any additional cases (household, business, etc.), to search for possible environmental sources of infection, and to recommend appropriate decontamination of the implicated environmental source of infection.

Upon receipt of a report of a Legionellosis case, contact the physician and/or hospital to confirm the diagnosis. Document laboratory test results.

In case of association in several cases investigate possible environmental source(s) of infection and identify additional cases

## **Prevention of transmission**

Prevention can be achieved by preventing the transmission from the environment to the human host. This method has proven useful to control outbreaks.

### Disinfection Methods

*Legionella* grows poorly at <20 °C and >50 °C and is killed at temperatures >60 °C. It is susceptible to chlorine and bromine disinfectants, ozone, heavy metal ions and UV. But the studies performed under lab conditions were not always successful in predicting effectiveness under field conditions.

Cooling towers and evaporative condensers: They can be disinfected by hyperchlorination, but safer approaches would be

- to place them away from public areas
- to use drift eliminators
- to clean from organic matter periodically
- to dose automatically a biocide

The following excerpt is from the ASHE Technical Document - Regulatory Advisory regarding addressing compliance with JCAHO standards (Utility Standards). These statements support biocide use as an industry standard: <http://www.ashe.org/media/water.html>

Cooling towers typically operate at 85°F - 95°F (with a range of 70 °F - 120 °F). Biofilms, which form at surfaces of heat exchanger, structure, and sump, serve as nutrients for *Legionellae* bacteria. Cooling towers should be designed and constructed so that tower drift is directed away from the hospital's air intake system and the volume or aerosol drift is minimized. For all operational cooling towers, hospitals should: Install drift eliminators Use an oxidizing biocide continuously to prevent the formation of biofilms and control biological growth. (E.g. bromine, chlorine, iodine, chlorine dioxide, ozone, etc.) And intermittently a non-oxidizing biocide (e.g. DBNPA, isothiazoline, etc.) Maintain towers according to manufacturers recommendations. If the tower/cooler is subject to seasonal shutdown, equipment should be cleaned and treated prior to shutdown and again before starting up the system for the first time in the season. Keep adequate maintenance records

### Hot water system

Flushing for >5mn at temperature >65 °C or hyperchlorination (flushing with water ≥10 mg/L free residual chlorine) have eliminated *Legionella*. However *Legionella* may grow back unless hot water is maintained at ≥50 °C and cold water at ≤20 °C or residual chlorine maintained at ≥1-2 mg/L of free chlorine. Hot water carries the risk of scalding users, hyperchlorination causes corrosion and leaks. If scale and sediments have accumulated in the system, replacement and physical cleaning may be necessary. UV, ozone and heavy metals have been tried with varying successes.

Nebulizer, respiratory therapy equipment: Use sterile water, do not let water stand, clean regularly.

Whirlpool spas: Maintain halogen levels at 4-10 mg/L and monitor levels frequently. pH should be maintained at 7.2-7.8 to ensure effective disinfection by halogens. Drain and clean system frequently (daily if heavy use). Replace filters regularly.

Surveillance: Some have taken the approach of monitoring the water quality and institute measures colonization with *Legionella* occurs but presence of *Legionella* does not often result in aerosol transmission. Sampling difficulties cause the result to poorly predict true concentration of *Legionella* in water

## **Hospital precaution and isolation: Standard precautions**